REMARKS

Interview

Applicants would like to thank Examiner Chang-Yu Wang and her Primary Examiner Christine Saoud for the phone conference held with Applicants' representative on October 23, 2007. During the phone interview, the Examiners proposed amendments to the claims for overcoming the rejections, especially the rejection under 35 U.S.C. § 103. Applicants have considered the proposed amendments and have incorporated a number of the proposed amendments into the claims.

The Examiners also agreed to consider Applicants arguments regarding the obviousness double patenting rejection in view of the fact that the claims directed to methods of using cell-free or membrane-free SV2 proteins were not allowed in U.S. Application 10/308,163 (U.S. Patent 7,090,985 because that application did not disclose a method of isolating cell-free or membrane-free SV2 proteins.

Status of the Claims

Claims 93-102, 139-142, 144-154, 156, 174-189 are currently pending in the present application. Claims 1-92, 103-138, 143, 155, and 157-173 have been canceled without prejudice or disclaimer of the subject matter claimed therein.

Amendments to the Claims

Claims 93, 139, and 156 have been amended as suggested by the Examiner during the phone interview. Support for the amendments to these claims can be found throughout the specification. Representative support can be found in claims 93, 139, and 156 and in Example 3, page 53, line 16 to page 55, line 17.

Claims 152, 153, 175, 180, 184, and 186 have been amended to correct inadvertent typographical errors.

The amendments to the claims do not introduce prohibited new matter.

Rejections Under 35 U.S.C. § 112, First Paragraph

A. Claims 93-102, 139-142, 144-154, 156, and 174-189 are rejected under 35 U.S.C. 112, first paragraph, because the specification allegedly does not enable the claimed invention.

The Office Action alleges that the specification does not enable all LEV derivatives and analogs that bind LEV binding site of the SV2A protein or all compounds that modulate all the different activities of all SV2 proteins as reasonably be useful for treating neurological diseases.

Without acquiescing to the propriety of this rejection and in view of Examiner's suggested amendments during the phone interview, claim 93 has been amended to include a step of comparing the binding of a compound or agent to the SV2 protein with the binding of LEV (or an analog or derivative thereof) to the SV2 protein in a control. Claims 139 and 156 have been amended to recite a method of identifying a compound or agent that binds a LBS of an SV2 protein. These amendments were suggested by the Examiners during the phone interview.

Applicants respectfully point out that the present invention provides novel methods of identifying new agents or compounds that bind an SV2 protein. The claims as they stand are directed to a method of identifying an agent or compound that binds an SV2 protein using LEV's (or an analog's or derivative's) binding to SV2 as a control or for comparison. The claims are neither directed to LEV derivatives and analogs nor directed to compounds that modulate all the different activities of all SV2 proteins.

Moreover, claim 93 and its dependent claims are directed to a method of identifying a compound or an agent that binds the LBS on an SV2 protein comprising determining whether the compound or agent binds the LBS on an SV2 protein by comparing its binding to SV2 protein with the binding of LEV (or an analog or derivative thereof) to the SV2 protein in a control sample. Since LEV is known to bind to the LBS of a SV2 protein, it is used as a control for comparison. Also, it is well-known that in such a control sample, the test compound would not be included. Claim 93 and its dependent claims include all the necessary steps. Thus, claim 93 and its dependent claims are enabled by the specification and should not be included under this rejection.

Moreover, Applicants respectfully submit that page 5 (second paragraph) of the Office Action, dated November 28, 2006, stated that Applicant is enabling for identifying a compound that binds SV2 protein (SV2A/B/C). Claim 93 and its dependent claims as they stand are

directed to a method of identifying an agent or compound that binds an SV2 protein. Accordingly, claim 93 and its dependent claims should not be included under this rejection, since the previous Office Action stated that the claimed invention of identifying a compound that binds an SV2 protein is enabled. Furthermore, published U.S. Application 20050137241, submitted with Applicants' response dated March 28, 2007, provides additional support that SV2C, in addition to SV2A, binds LEV.

Claims 139 and 156 are also directed to methods of identifying a compound or an agent that binds the LBS on an SV2 protein comprising using LEV (or analog or derivative thereof) to compete with the test compound or agent for binding to the SV2 protein. If the binding of LEV to the LBS of the SV2 protein is inhibited by the compound or agent, then the test compound or agent also binds the LBS on the SV2 protein. It is within the skill of a person of ordinary skill in the art to determine how to assess inhibition of binding. For example, inhibition of binding may be determined by comparing to a control sample which does not contain the test compound or agent. The specification on pages 20-26 discloses various other methods for determining inhibition of binding. Thus, 139 and 156 and their dependent claims include all the necessary steps and are enabled by the specification.

The Office Action noted that US20050137241 was filed on November 30, 2004 and states that enablement is determined based on the application at the time it was filed. However, Applicants submit that US20050137241 was submitted in the previous response to support the teachings of the specification that SV2 proteins bind LEV. As discussed in the previous Office Actions, SV2 proteins are structurally and functionally related proteins as evidenced by Janz *et al.* (Neuroscience, 1999, 94(4): 1279-1290, submitted September 13, 2006). This reference was published before the priority date of the present application. Accordingly, since SV2 proteins have been characterized and since the specification teaches and the relevant art shows that LEV and its analogs or derivatives bind SV2 proteins, the specification enables each of the steps encompassed by the claims and the claimed invention of identifying compounds or agents that bind SV2 proteins.

Applicants respectfully point out that the specification enables the claimed methods of identifying compounds or agents that bind the LBS of an SV2 protein. The specification teaches binding assay and competition assay using LEV binding to an SV2 protein as a control or for

comparison. As an example, pages 20-26 disclose various methods of identifying agents of compounds using LEV as a control. Moreover, the Examples also provide various binding assays using LEV and an SV2 protein.

The Office Action also alleges that the specification does not enable all LEV analogs/derivatives binding to LBS of an SV2 protein. Applicants respectfully point out that the claims are directed to methods of identifying agents and compounds that bind the SV2 protein and that the claims are not directed to LEV analogs/derivatives. Moreover, using the claimed methods, Applicants have identified a number of LEV analogs/derivatives that bind an SV2 protein as evidenced in the attached references (WO 2007/065595, WO 2006/128693, WO 2005/118561, WO 2004/087658, and WO 2002/094787). The attached references are provided to support the specification's enablement of the claimed invention.

The Office Action has not provided a reasonable explanation as to why the scope of the claims are not adequately enabled by the specification and has not provided evidence showing that the claims as they stand are not enabled by the specification. The court in *In re Marzocchi* stated that it is incumbent upon the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). In the absence of evidence to the contrary, Applicants respectfully request withdrawal of the rejection.

Obviousness-Type Non-Statutory Double Patenting Rejection

Claims 93-102, 139-142, 144-154, 156, and 174-189 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 9-12, 17-19, 22-25, 29, 35, 37-40, 45-52, 54-57, 61-68, 71-74 and 78 of U.S. Patent 7,090,985 ('985).

The claims as they stand are directed to a method of identifying an agent that bind an SV2 protein. One of the steps comprises obtaining a cell-free or membrane-free SV2 protein. SV2 proteins contain twelve transmembrane domains and are difficult to isolate in cell-free or membrane-free functionally active form. Thus, the routinely disclosed methods for solubilizing transmembrane domain proteins would not be expected to be effective in isolating and purifying

SV2 proteins. Applicants discovered a way of obtaining SV2 proteins in cell-free or membrane-free form without inactivating the proteins. The method is described in detail in the specification. Accordingly, the claims include the step of obtaining a cell-free or membrane-free SV2 protein.

In contrast, the claims of U.S. Patent '985 are directed to a method of identifying a binding partner for SV2A protein comprising providing a recombinant host cell expressing the SV2A protein and incubating the host cell with a test agent and LEV or an analog or derivative thereof. The claims of U.S. Patent '985 also include obtaining a cellular preparation from the host cell and incubating the cellular preparation with a test agent and LEV or an analog or derivative thereof. The claims of U.S. Patent '985 do not require obtaining a cell-free or membrane-free SV2 protein.

Moreover, Applicants respectfully point out that in U.S. Patent 7,090,985, claims directed to methods of using cell-free or membrane-free SV2 proteins were not allowed because the Examiner alleged that Applicants have not enabled purifying the SV2 protein from the membrane of a cell.

The Office Action alleges that there is substantial overlap in scope in the present application and '985 and the test compounds can be antibodies, analogs/derivatives of levetiracetam or any molecules that can compete with or modulate the binding of levetiracetam to an SV2A protein. Although the test compounds that can be identified using the claimed methods of the present application and '985 may overlap, the claimed methods of the present application and '985 are not obvious variants of each other. The claimed methods of the present application require obtaining a cell-free or membrane free SV2 protein, while the methods of '985 do not require such a step. As discussed above, since SV2 proteins contain 12 transmembrane domains, it is difficult to obtain these proteins in cell-free or membrane-free functionally active forms.

The Office Action alleges that WO 2003016475 teaches that the use of cell-free or membrane-free polypeptides in high throughput screening assays is routine practice. Although WO 2003016475 generally teaches solubilizing membrane bound proteins, the reference does not teach isolating cell-free or membrane-free SV2 proteins containing twelve transmembrane domains for use in screening assays. The isolation of cell-free or membrane-free SV2 proteins is

not routine practice, since SV2 proteins contain twelve transmembrane domains. Accordingly, WO 2003016475 does not render the claimed invention obvious.

Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejections Under 35 U.S.C. § 103

Claims 93-102, 139-142, 144-154, 156, and 174-189 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO2003016475 (WO '475) in view of Margineanu *et al.* (Margineanu) and Berkower.

Applicants respectfully point out that the Office Action incorrectly summarized Applicants' position on page 16 of the response dated March 28, 2007. In the response dated March 28, 2007, Applicants did not state that WO '475 teaches cell free screening assays. Rather, Applicants stated in the previous response that WO '475 does not teach how to obtain cell-free or membrane-free SV2 proteins and that SV2 proteins are difficult to obtain in cell-free or membrane-free form because they contain twelve transmembrane domains. Applicants also stated in the previous response that WO '475 discloses the amino acid sequence of SV2A in its Sequence Listing as one of the three thousand or so sequences and that the reason for the disclosure of SV2 protein sequence in WO '475 is not known.

The Office Action alleges that WO '475 teaches cell-free high throughput screening methods. Applicants submits that even if WO '475 teaches cell-free high throughput screening methods, WO '475 does not render the claimed invention obvious because WO '475 does not teach how to obtain cell-free and membrane-free form of proteins having twelve transmembrane domains. Accordingly, there is no reasonable expectation of success in isolating SV2 proteins from a cell membrane by following the general information provided by WO '475 for solubilizing membrane bound proteins. Moreover, WO '475 does not teach LEV binds SV2 proteins. WO '475 does not teach using LEV binding SV2 protein for comparison in determining whether a test agent or compound binds SV2 and does not teach competition assays using LEV to determine whether a test agent or compound competes effectively with LEV for binding the LBS of SV2 and therefore inhibits the binding of LEV to the LBS of SV2.

The secondary references do not cure the deficiencies of WO '475. Margineanu and Berkower do not disclose LEV binds SV2 proteins and do not teach competition assays using LEV or assays that include the step of comparing the binding of the test compound or agent to an

SV2 protein with the binding of LEV to the SV2 protein. Moreover, these secondary references neither disclose assays using cell-free or membrane-free SV2 proteins nor provide guidance for isolating SV2 proteins from cell membranes for use in screening assays to identify new compounds or agents that bind SV2 proteins. Accordingly, since neither the primary nor the secondary references teach that LEV binds SV2 proteins, there is no motivation to combine the three references. Also, since the secondary references do not cure the deficiencies of the primary reference, the combination of the three references would not render the claimed invention obvious.

The Office Action alleges that the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Applicants respectfully submit that the claims as they stand require obtaining cell-free or membrane-free SV2 proteins and either comparing the binding of the agent or compound to an SV2 protein with the binding of LEV to the same SV2 protein or having the agent or compound compete with LEV for binding to the LBS of an SV2A protein. However, there is no reasonable expectation of success in obtaining cell-free or membrane-free SV2 proteins based on the general disclosure of WO '475 for solubilizing membrane bound proteins, since SV2 proteins contain twelve transmembrane domains. Additionally, the cited references do not teach that SV2 proteins interact with LEV. Thus, one would not reasonably expect LEV to bind SV2 proteins or to compete with other agents for binding SV2A protein. Thus, there is no motivation to combine the cited references and to modify the teachings of the cited reference to obtain each of the steps of the claimed method. Thus, the cited references do not render the claimed invention obvious.

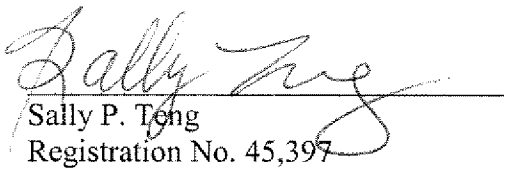
Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should an interview be helpful to further prosecution of this application, the Examiner is invited to telephone the undersigned.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time

under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
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